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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,695	11/21/2003	Leong Ng	ISA-012.01	1345

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EXAMINER
ROONEY, NORA MAUREEN

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,695	NG, LEONG	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,16,17 and 22-25* is/are pending in the application.

4a) Of the above claim(s) *22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 16-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/11/2007 has been entered.

2. Claims 1-7, 16-17 and 22-25 are pending.

3. Claims 22-25 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-7 and 16-17 are currently under examination as they read on a method for detecting tissue hypoxia.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains; or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7 and 16-17 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification, while being enabling for: a method for detecting tissue hypoxia in a mammalian subject comprising contacting a bodily fluid sample of said subject with anti-ORP 150 antibody and determining the level of ORP 150 protein

(SEQ ID NO:2) in said bodily fluid sample, including plasma, whereby an elevated level of ORP 150 relative to normal is indicative of an increased risk of heart disease that is the result of heart failure, chronic heart failure, coronary artery disease, ischaemic cardiomyopathy, myocardial infarction atherosclerosis, ischaemic stroke, aortic aneurysm or peripheral vascular disease; the method using lateral flow immunoassay or flow-through immunoassay with monoclonal antibodies specific for ORP 150; the method for detecting tissue hypoxia in a mammalian subject further comprising detection the BNP or N-BNP second marker in a bodily fluid sample of a mammal, including plasma, whereby an elevated level of the second marker is indicative of heart disease using lateral-flow immunoassay or flow through immunoassay; and the method for detecting tissue hypoxia in a mammalian subject wherein ORP 150 and/or the second marker are monitored periodically, does not reasonably provide enablement for: a method for detecting tissue hypoxia in a mammalian subject by (a) contacting a bodily fluid sample with an antibody specific for an oxygen related protein 150 (ORP 150) comprising SEQ ID NO: 2 in order to detect the level of ORP 150 in the bodily fluid sample, whereby an elevated level of ORP 150 relative to normal is indicative of an increased risk of heart disease and (b) contacting a bodily fluid sample with an antibody specific for **brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)**, whereby an elevated level of **brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)** is indicative of an increased risk of heart disease of claim 1; wherein heart disease is the result of heart failure, chronic heart failure, coronary artery disease, ischaemic cardiomyopathy, myocardial infarction atherosclerosis, ischaemic stroke, aortic aneurysm, or peripheral vascular disease of claim 2; wherein the bodily fluid is plasma of claim 3; wherein the method is an immunoassay of claim 4;

wherein the immunoassay is a lateral flow immunoassay of claim 5; wherein the immunoassay is a flow-through immunoassay of claim 6; wherein the antibody is a monoclonal antibody of claim 7; wherein the level of ORP 150 is monitored periodically of claim 16; and wherein the level of **brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)** is monitored periodically for the same reasons as set forth in the Office Action mailed on 11/16/2006.

The specification is not enabled for the use of any "N-BNP" or "BNP" polypeptide without reference to a specific polypeptide sequence for the recited "N-BNP" or "BNP."

Applicant argues that the terms "BNP" and "N-BNP," and how to make and use BNP and N-BNP, is supported throughout the specification, both verbatim and by incorporating by reference articles describing BNP and N-BNP (see, e.g., page 1, page 6, pages 9-10, etc.) A sequence of BNP or N-BNP is not necessary for one of skill in the art to be able to detect BNP or N-BNP in a sample; methods for doing so and reagents for doing so are well- known and widely available in the art. N-BNP is derived from the precursor of BNP and is considered a reasonable alternative to using BNP in diagnosing conditions such as LVSD. Thus, although the working examples in the specification illustrate the successful use of N-BNP in conjunction with ORP 150, it would not constitute undue experimentation for one of skill in the art to adapt the assays for use with BNP instead.

It is the Examiner's position that BNP and N-BNP are not disclosed in the specification, such as by a specific sequence identifier, such that one would be able to practice the claimed

invention without undue experimentation. Applicant asserts that the publications describing the N-BNP and BNP are incorporated by reference. However, contrary to Applicant's assertion, the incorporation by reference of the sequences for N-BNP and BNP requires a sequence listing, CRF and statement that the sequence listing and CRF are the same including the additional sequences for the sequences for BNP and N-BNP to be properly incorporated.

7. Claims 1-7 and 16-17 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a method for detecting tissue hypoxia in a mammalian subject comprising contacting a bodily fluid sample of said subject with anti-ORP 150 antibody and determining the level of ORP 150 protein (SEQ ID NO:2) in said bodily fluid sample, including plasma, whereby an elevated level of ORP 150 relative to normal is indicative of an increased risk of heart disease that is the result of heart failure, chronic heart failure, coronary artery disease, ischaemic cardiomyopathy, myocardial infarction atherosclerosis, ischaemic stroke, aortic aneurysm or peripheral vascular disease; the method using lateral flow immunoassay or flow-through immunoassay with monoclonal antibodies specific for ORP 150; the method for detecting tissue hypoxia in a mammalian subject further comprising detection the BNP or N-BNP second marker in a bodily fluid sample of a mammal, including plasma, whereby an elevated level of the second marker is indicative of heart disease using lateral-flow

immunoassay or flow through immunoassay; and the method for detecting tissue hypoxia in a mammalian subject wherein ORP 150 and/or the second marker are monitored periodically.

Applicant is not in possession of: a method for detecting tissue hypoxia in a mammalian subject by (a) contacting a bodily fluid sample with an antibody specific for an oxygen related protein 150 (ORP 150) comprising SEQ ID NO: 2 in order to detect the level of ORP 150 in the bodily fluid sample, whereby an elevated level of ORP 150 relative to normal is indicative of an increased risk of heart disease and (b) contacting a bodily fluid sample with an antibody specific for **brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)**, whereby an elevated level of **brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)** is indicative of an increased risk of heart disease of claim 1; wherein heart disease is the result of heart failure, chronic heart failure, coronary artery disease, ischaemic cardiomyopathy, myocardial infarction atherosclerosis, ischaemic stroke, aortic aneurysm, or peripheral vascular disease of claim 2; wherein the bodily fluid is plasma of claim 3; wherein the method is an immunoassay of claim 4; wherein the immunoassay is a lateral flow immunoassay of claim 5; wherein the immunoassay is a flow-through immunoassay of claim 6; wherein the antibody is a monoclonal antibody of claim 7; wherein the level of ORP 150 is monitored periodically of claim 16; and wherein the level of **brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)** is monitored periodically of the same reasons as set forth in the Office Action mailed on 11/16/2006.

BNP and N-BNP are not described in adequate detail in the specification, such as by a specific sequence identifier.

Applicant's arguments filed on 10/11/2007 have been fully considered, but are not found persuasive.

Applicant argues that to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. As argued above, Applicants have clearly described in the specification what is meant by "N-BNP" and "BNP" in detail and by incorporation by reference. A sequence of BNP or N-BNP is not necessary for one of skill in the art to be able to detect BNP or N-BNP in a sample; methods for doing so and reagents for doing so are well-known and widely available in the art. Most references describing an assay for detection of BNP or N-BNP do not provide the sequence of either molecule, yet there is no doubt the authors had possession of the disclosed assay. Applicants have reduced to practice at least one assay for N-BNP, and have described other species in the genus of what is BNP and N-BNP in sufficient detail such that one of skill in the art would know what was meant by the terms.

BNP and N-BNP are not described in adequate detail in the specification, such as by a specific sequence identifier. Applicant asserts that the publications describing the N-BNP and BNP are incorporated by reference. However, contrary to Applicant's assertion, the incorporation by reference of the sequences for N-BNP and BNP requires a sequence listing,

CRF and statement that the sequence listing and CRF are the same including the additional sequences for the sequences for BNP and N-BNP to be properly incorporated.

Claim Rejections - 35 USC § 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-4, 7 and 16-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,948,637 in view of Hall et al. (PTO 1449 filed 6/18/2004, Reference AG) for the same reasons set forth in the Office Action mailed on 11/16/2006.

The 637' patent claims the purified human ORP-150 protein of SEQ ID NO: 1 (identical to SEQ ID NO: 2 of the instant application over length and sequence), monoclonal antibodies to the ORP 150 protein and a method of diagnosis of ischemic diseases in a patient by detecting the ORP 150 polypeptide that is induced under hypoxic conditions (In particular, abstract, column 1 lines 41-67, column 2 lines 11-14, column 4 lines 46-67 and column 5 lines 1-12).

The prior art differs from the claimed invention by the recitation of detection of ORP-150 in a bodily fluid sample (Claim 1) such as plasma (Claims 3 and 14) by immunoassay (Claim 4)

and by detection of a second marker indicative of an increased risk of heart disease (Claim 8) by immunoassay (Claim 11) and monitoring over a series of timepoints (Claims 16-17).

Hall et al. teaches detection of natriuretic peptide, particularly N-terminal pro-brain natriuretic peptide (N-BNP) and brain natriuretic peptide (BNP), in the diagnosis and management of heart failure patients. The reference teaches that the determinations should be combined with other diagnostic examinations, including other peptide determinations to improve diagnostic performance and that it can be done over a series of time points to better monitor disease (In particular, page 395, fourth paragraph, page 396, fourth paragraph and page 397, last paragraph). The reference also teaches the ease of detecting the proteins in a patient's plasma (In particular, page 395, third paragraph and page 396, first and last paragraphs) and detection by immunoassay (In particular, pages 395, second paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect ORP 150 protein in a patient to detect increased risk of heart disease in bodily fluid, such as plasma, using monoclonal antibodies to the ORP-150 protein (637' patent) in an immunoassay (Hall et al.) because immunoassays are specific, reliable and convenient to use. Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for an assay.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine the determination of ORP 150 (637' patent) with the determinations of other

diagnostic markers, such as BNP and N-BNP, for diagnosis of heart failure (Hall et al.), in view of the suggestion in Hall et al. to combine tests to improve diagnostic performance. It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to detect the level of ORP 150 alone or in combination with a second marker to better adjust a patient's therapy according to their cardiac disease and severity associated peptide levels, as suggested by Hall et al. (In particular, page 396, third paragraph and page 396, second paragraph).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 10/11/2007 have been fully considered, but are not found persuasive.

Applicant argues that the '637 patent does not teach or suggest a method for detecting tissue hypoxia in a mammalian subject by contacting a bodily fluid sample with an antibody specific for an oxygen related protein 150 (ORP 150) comprising SEQ ID NO: 2 in order to detect the level of ORP150 in the bodily fluid sample, whereby an elevated level of ORP150 relative to normal is indicative of an increased risk of heart disease. Hall is relied on by the Examiner as teaching the detection of natriuretic peptide, particularly in combination with other diagnostic tests.

Applicants respectfully assert that the Examiner has misconstrued the teachings of Hall. Hall discusses in section 7 whether the natriuretic peptide measurements would make other diagnostic examinations superfluous and discusses whether the natriuretic peptide measurements could replace the existing gold standard or only be used to supplement current methods. Thus, it does not teach or suggest the desirability of combining the natriuretic peptide measurements with *any* other diagnostic that might be developed later on, nor does it teach or suggest the mode, e.g. using a computer program (logistic regression analysis), by which the two measurements could be combined. Further, it is not obvious why measurement of a protein increased by hypoxia combined with another protein increased in heart failure would provide for an improvement in accuracy of the diagnostic; such a combination would not have afforded predictable results. Hall does not provide any insight into this issue. Applicants respectfully submit that based on the teachings of Hall, one of skill in the art would not have been motivated to combine a completely novel diagnostic based on another protein as taught in the '637 patent.

It is the Examiner's position that instant claim 1-4, 7 and 16-17 are unpatentable over the 637' patent in view of the Hall et al. reference because each limitation is taught between the two references. The '637 patent teaches the detection of ORP150 comprising SEQ ID NO:2 which is induced under hypoxic conditions to diagnose ischemic disease and Hall et al. teaches the detection of natriuretic peptides in the diagnosis and management of heart failure patients. The idea of an assay combining detection of the two flows logically from their having been individually taught in the prior art. Further, Hall et al. explicitly suggests combining the natriuretic peptide measurements with other diagnostics.

Thus, it would be obvious to one of ordinary skill in the art at the time the invention was made to combine the determination of ORP 150 (637' patent) with the determinations of other diagnostic markers, such as natriuretic peptides, for diagnosis of heart failure (Hall et al.), in view of the suggestion in Hall et al. to combine tests to improve diagnostic performance. It is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Applicant's assertion that the Examiner has misconstrued Hall et al. because Hall et al. does not teach that natriuretic peptide measurements could be combined with any other diagnostic that might be developed later or the mode by which the measurements could be combined is without merit. Hall et al. teaches that natriuretic peptide measurements can be

combined with other diagnostics. There is no requirement that Hall et al. explicitly teach any further motivation. Section 7 in Hall et al discussing whether natriuretic peptide measurements make other diagnostic examinations superfluous and whether they could replace the existing gold standard or only be used to supplement current methods, does not undermine the fact that Hall et al. discusses that natriuretic peptide measurements can be used in combination with other diagnostics. The method need not be a sufficient diagnostic method that replaces the gold standard, it need only be used for the recited purpose as a combined diagnostic. Further, contrary to Applicants assertion, it is obvious to measure a protein increased by hypoxia and another protein increased in heart failure because they are both hypoxic conditions. It would necessarily provide for an improvement in accuracy of the diagnostic because they are measuring the same condition and such a combination would have afforded predictable results.

10. Claims 4-5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,948,637 in view of Hall et al. (PTO 1449 filed 6/18/2004, Reference AG) as applied to Claims 1-4, 7 and 16-17 above, and further in view of Karl et al. (PTO-1449 filed 6/18/2004, Reference AJ) for the same reasons as set forth in the Office Action mailed on 11/16/2006.

The teachings of the 637' patent and Hall et al. have been discussed *supra*.

Claim 5 differs from the prior art by the recitation of detection of ORP 150, BNP and N-BNP using lateral flow immunoassay.

Karl et al. teaches immunoassay reagents and methods for measurement of natriuretic peptides in blood and plasma for diagnosis of cardiac impairment (In particular, abstract, introduction, and page 180, last paragraph). The reference teaches using a sandwich assay to detect NT-proBNP, which is a lateral flow immunoassay as defined in the instant specification.

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150, BNP and N-BNP in a patient's bodily fluid, such as plasma, using monoclonal antibodies to the ORP 150 and, BNP and N-BNP (637' patent) in a lateral flow immunoassay (Karl et al.) to detect increased risk of heart disease. Lateral flow immunoassays, such as sandwich format immunoassays, are efficient " highly sensitive" and "specific" (In particular, page 177, abstract). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

It would be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 and BNP or N-BNP with a lateral flow immunoassay because it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the combined teachings of the references, it is apparent that one of ordinary skill in

the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 10/11/2007 have been fully considered, but are not found persuasive.

Applicants argue that as discussed above, the combination of the '637 patent with Hall does not render claims 1-4, 7 and 16-17 obvious. The addition of Karl et al does not remedy this deficiency.

Examiner's position on the teachings of the 637' patent and Hall et al. has been discussed *supra*. It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein, N-BNP and BNP in a patient's bodily fluid, such as plasma, using antibodies to the polypeptides in a lateral flow immunoassay (Karl et al.) to detect increased risk of heart disease because lateral flow immunoassays, such as sandwich format immunoassays, are efficient " highly sensitive" and "specific" (In particular, page 177, abstract).

11. Claims 4 and 6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,948,637 in view of Hall et al. (PTO 1449 filed 6/18/2004, Reference AG) as applied to

Claims 1-4, 7 and 16-17 above, and further in view of May et al. (PTO-892, Reference A) for the same reasons as set forth in the Office Action mailed on 11/16/2006.

The teachings of the 637' patent and Hall et al. have been discussed *supra*.

Claim 6 differs from the prior art by the recitation of detection of ORP 150, BNP and N-BNP using flow-through immunoassay.

May et al. teaches a specific, flow-through immunoassay for determining pregnancy that reacts a liquid biological sample with a test strip made of dry porous material that absorbs the liquid biological sample and transports the biological sample to a membrane zone with immobilized antibody to hCG. If the antigen is present in a biological sample, a colored spot develops on the surface of the membrane through use of a color tagged secondary antibody. (In particular, Claims 1-34 and column 2 lines 3-20).

It would also be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150, BNP and N-BNP in a patient's bodily fluid, such as plasma, using monoclonal antibodies to ORP 150, BNP and N-BNP (637' patent, Hall et al.) in a flow-thorough immunoassay (May et al.) to detect increased risk of heart disease. The May et al. reference teaches that such a device is optimal as it is specific, reliable, quick, convenient, commercially available and suitable for home-use because of the lack of requisite skill and ease of obtaining a bodily fluid sample for use (In particular column 1 lines 10-45 and lines 64-67 and

column 2, lines 1-2). Bodily fluids such as plasma are convenient to obtain from a patient and contain all the requisite proteins necessary for performing such an assay.

It would be obvious to one of ordinary skill in the art at the time the invention was made to detect ORP 150 and BNP or N-BNP with a lateral flow immunoassay because it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed on 05/21/2007 have been fully considered, but are not found persuasive.

Applicants argue that the combination of the '637 patent with Hall does not render claims 1-4, 7 and 16-17 obvious. The addition of May et al does not remedy this deficiency.

It is the Examiner's position that it would be obvious to one of ordinary skill in the art at the time the invention was made to combine detection of ORP 150 protein, N-BNP and BNP in a patient's bodily fluid, such as plasma, using antibodies to the polypeptides in a flow-thorough immunoassay (May et al.) to detect increased risk of heart disease because the May et al. reference teaches that such a device is optimal as it is specific, reliable, quick, convenient, commercially available and suitable for home-use because of the lack of requisite skill and ease of obtaining a bodily fluid sample for use (In particular column 1 lines 10-45 and lines 64-67 and column 2, lines 1-2).

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 23, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

Technology Center 1600

Maher M. Haddad

MAHER M. HADDAD
PRIMARY EXAMINER